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IGF-I Polymorphism is Associated with Lean Mass, Exercise Economy and Performance Among Premenopausal Women

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Abstract

Background—We undertook this study to investigate the association of a genetic polymorphism of the insulin-like growth factor, IGF-I₁₈₉, on body composition, exercise performance and exercise economy, after controlling for the independent effect of race as assessed by African genetic admixture (AFADM).

Methods—A total of 114 premenopausal sedentary women were genotyped for IGF-I₁₈₉, obtaining measures of fat mass, lean body mass, VO₂ during cycling and stairclimbing, time on treadmill and leg strength. A quantitative value for AFADM was derived from genotypic information of approximately 40 ancestry informative markers and used as covariate in statistical models.

Results—After adjusting for AFADM, IGF-I₁₈₉ was negatively associated with lean body mass ($p = 0.029$) and lean leg mass ($p = 0.050$). Leg strength was not associated with the presence/absence of IGF-I₁₈₉ ($p = 0.380$), but carriers of the allele demonstrated a longer time on the treadmill ($p = 0.015$) after adjusting for AFADM. There was also a negative relationship between oxygen uptake during cycling and presence of the IGF-I₁₈₉ independent of AFADM ($p = 0.010$).

Conclusion—Independent of AFADM, individuals with IGF-I₁₈₉ are more likely to have low leg lean mass and to perform better in activities requiring exercise economy and endurance performance.

Keywords

Genetic admixture; VO₂; Racial differences; Strength; Endurance; IGF-I polymorphism

Introduction

Insulin-like growth factor-I (IGF-I) is an important regulator of many aspects of cell growth and differentiation, playing a critical role in mediating the growth of cartilage, bone, muscle

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and other tissues (1). IGF-I increases muscle protein content, reduces degradation, promotes skeletal muscle hypertrophy, and is also an important factor for an adequate muscle glucose uptake since it is closely related with insulin sensitivity (2,3). Levels of IGF-I in plasma have been positively associated with muscle mass and strength in humans (4). It is clear that the role of IGF-I in muscle metabolism is of critical importance and that alterations in its action may result in insulin resistance and lower muscle performance. Polymorphisms in genes of the insulin-like growth factor (IGF) system are associated with variations in several aspects of metabolism that might result in obesity or other pathological conditions. Variants in IGF-I have been associated in humans with obesity-related parameters (5–7); genetic variation in the IGF-II gene has been found associated with a decrease in insulin sensitivity; and subjects with a polymorphism in the IGF binding protein I (IGFBPI) gene have been reported to accumulate more visceral fat (8). Thus, it appears that variation in the genes of the IGF system may explain, to a certain degree, variability in some components of physiology and body composition.

The role of IGF-I polymorphisms in obesity-related measures is not completely clear. Research has indicated that a variant in the IGF-I gene, the CT repeat of 189-bp allele (IGF-I₁₈₉), is associated with lower body mass index (BMI), fat mass (FM) and fat-free mass (FFM) in humans (9). In a study testing responses to dietary intake, no significant effect on body composition was observed between homozygotes for IGF-I₁₈₉ (189/189) and homozygous non carriers (NC/NC) after a period of 100 days of overfeeding (8). Studies exploring the effect of 20 weeks of endurance exercise in IGF-I₁₈₉ carriers have demonstrated that homozygous 189/189 individuals have a lower increase in FFM than heterozygous individuals or noncarriers (NC) of the allele (9). The results of these investigations suggest that IGF-I₁₈₉ could have an effect on the development of FFM.

One of the concerns of genetic association studies is the confounding effect of population stratification. Racial categorization is a significant confounder in genetic associations, particularly because of the multiple factors underlying its categorization (physiological, genetic and behavioral), and their contribution to the etiology of a disease. One approach to tease apart genetic, environmental and behavioral components of race is to control for genetic admixture, where a quantitative value representing the degree of ancestral information in an individual is obtained based on ancestry informative genetic markers. This approach allows the decomposition of biological components of racial/ethnic classification, provides statistical power by assigning individuals a value within a range of 0–100 rather than limiting them to a category, and reduces the confounding of population stratification. Genetic admixture has been successfully used to explore population differences in metabolic and physiological parameters (10,11), and it represents a reliable method to study the effect of IGF-I₁₈₉ independently of the genetic aspect of racial classification.

In this study we investigated the relationship of the IGF-I₁₈₉ polymorphism with body composition, exercise performance and exercise economy in premenopausal sedentary women, controlling for the genetic component of race through the use of African genetic admixture. Particular attention has given to the exploration of whether differences in lean mass also result in functional differences between IGF-I will contribute to reduced lean mass polymorphisms. We hypothesize that IGF-I₁₈₉ in individuals and that will have an effect on exercise-related outcomes.

Methods

Subjects

A total of 114 sedentary premenopausal women with a BMI range of 24–30 kg/m² and an age range of 25–46 years participated in the study, 70 were African Americans (AA) and 44 were European Americans (EA). Subjects belong to two ongoing longitudinal studies on the role of

metabolism in the etiology of obesity conducted in AA and EA premenopausal women. At the time of testing, participants had no previous history of exercise training and had no previous or undergoing intervention that affected body composition. All testing was performed in the follicular phase of the menstrual cycle. Women were weight stable for 1 month prior to testing and were on a controlled diet providing 20–22% of energy as fat, 16–23% as protein, and 55–64% as carbohydrate for 2 weeks before testing. Subjects were admitted to the General Clinical Research Center (GCRC) 3 days prior to testing. Only baseline data were considered for the study. Before participating in the study, the women provided informed consent to the protocol, which was approved and followed regulations by the Institutional Review Board for human use at the University of Alabama at Birmingham.

Body Composition

Measures of total fat mass (FM) and nonbone lean body mass (LBM) were obtained from body composition analysis using dual-energy X-ray absorptiometry (DPX-L; Lunar Radiation Corp, Madison, WI), software version 1.33 (Lunar Corp), following standard procedures. Arm fat mass (ARMFAT) was calculated by multiplying the DXA value for arm tissue in kg by the DXA value for arm percent tissue fat divided by 100. A similar approach was used to calculate leg fat mass (LEGFAT), nonbone arm (ARMLM) and leg lean mass (LEGLM).

Exercise Performance

Prior to the maximal exercise tests, all subjects underwent at least two equipment familiarization sessions. In the context of this study, endurance time (TREADTIME) was considered to be the time spent on the treadmill during the $\text{VO}_{2\text{max}}$ test. A measure of $\text{VO}_{2\text{max}}$ was determined during a maximal modified Bruce graded treadmill protocol (12). Heart rate was measured using a POLAR Vantage XL heart rate monitor (Gays Mills, WI). Oxygen consumption and carbon dioxide production were measured continuously via open circuit spirometry, and analyzed using a sensormedics metabolic cart (Model #2900, Loma Linda, CA). Prior to each test, the gas analyzers were calibrated with certified gases of known standard concentrations. Standard criteria for heart rate (keeping heart rate within 10 beats of age-predicted maximum), respiratory exchanged ratio (respiratory quotient of at least 1.10), and plateauing (an increase of less than 0.8 $\text{mlO}_2/\text{kg}/\text{min}$ when grade increased 2.5% of a speed of 3.0 mph) were used to ensure achievement of $\text{VO}_{2\text{max}}$ (13). All subjects achieved at least two criteria for $\text{VO}_{2\text{max}}$.

Leg strength (LEGSTR) was defined as the strength required for isometric knee extension at 110-degree extension while subjects were seated and the leg and upper torso were strapped to the chair to prevent hip movement. The validity of this test has been demonstrated elsewhere (14) and a recent study has shown a highly significant relationship between maximal voluntary contraction and muscle cross-sectional area (15). Force was measured with a universal shear beam cell (LCC 500, Omega Engineering, Stamford, CT). A digital transducer (DT2000, Omega Engineering) gave instantaneous force measurement feedback to the subject. After three practice trials, three maximum isometric contractions were recorded. The average of the two highest maximum forces generated were used for statistical purposes (16).

Exercise Economy

Measures of exercise economy were obtained by measuring submaximal VO_2 during stairclimbing and cycling. Submaximum oxygen uptake (VO_2) was obtained in the steady-state, during the third and fourth minutes of a stairclimbing (7" step, 60 steps/min, 4 min) and cycling (bicycle ergometer, 50-W workload, 4 min) task. Values representing oxygen uptake for stairclimbing (STAIR VO_2) and cycling (BIKE VO_2) were obtained by averaging the VO_2 during the steady-state for each exercise (adjusted for body mass and expressed in $\text{ml}/\text{kg}^{-1}\text{min}^{-1}$) and subtracting from that value the VO_2 value during resting. Since the cycling

task entailed an absolute workload of 50 W (rather than one that was dependent on bodyweight), an absolute value for bike VO_2 was created (BIKEVO2-A) by multiplying by bodyweight and expressed in $\text{ml}/\text{min}^{-1}$.

Genotyping

Variants for IGF-I were obtained by genotyping a polymorphic (CT)_n repeat that begins at base pair 140 of the human gene on chromosome 12q23 (17,18) using the polymerase chain reaction as described elsewhere (19). Products were separated using capillary electrophoresis (ABI310) and sized using GeneScan software. To decompose the biological and non-biological aspects of race, we used admixture instead of racial classification as a covariate in statistical models. This approach relies on the estimation of a quantitative value based on information from markers across the human genome that are informative for parental ancestry, defined as those long-separated populations that intermixed during historical periods to produce new admixed populations. Genotyping for the measures of genetic admixture was performed at The Pennsylvania State University using the McSNP method (20) and agarose gel electrophoresis. Molecular techniques for the allelic identification and methodology for genetic admixture application have been described elsewhere (10,11,21,22). Approximately 40 ancestry informative markers were utilized for the study, as described by Shriver et al. (23) Information regarding marker sequences, experimental details, and parental population allele frequencies has been submitted to dbSNP (<http://www.ncbi.nlm.nih.gov/SNP/>) under the handle PSU-ANTH.

Statistical Methods

The statistical models were based on two types of associations: allelic and genotypic. Allelic information referred to the presence or absence of IGF-I₁₈₉ and was categorized and dummy coded according to presence (1) or absence (0) of the allele. Genotypic information referred to the diploid pattern of combination of alleles in each subject and was classified into three categories: those having two copies of IGF-I₁₈₉ (189/189), those having no copies of the IGF-I₁₈₉, or non carriers (NC/NC) and those having only one copy of the IGF-I₁₈₉ (189/NC). In the dummy coding system for the genotypic association statistical model, the coding 0, 1 was used for genotypic combination 189/NC; coding 1, 0 was used for 189/189; and coding 0, 0 was assigned for NC/NC.

A chi-square test with two degrees of freedom was used to test for differences in genotypic frequencies between EA and AA individuals. Analysis of variance (ANOVA) and a Duncan post hoc test were used to test for differences in the variables of interest according to genotype.

Two linear regression models were used for data analyses: one where the dependent variable was regressed on the presence or absence of the IGF-I₁₈₉ allele (allelic associations), and another where the dependent variable was regressed on the genotypic combinations 189/189, 189/NC or NC/NC (genotypic associations). In the genotypic association models the homozygote NC/NC (dummy coding 0, 0) represented the intercept. Potential confounding variables were included as covariates, as appropriate. Every statistical model was evaluated with and without African genetic admixture as a covariate. All the analyses were performed using the general linear model procedure of SAS, version 8 (SAS Institute, Cary, NC).

Results

Table 1 shows the allelic distribution of the polymorphic (CT)_n repeat of IGF-I. The frequency of the IGF-I₁₈₉ allele in the entire sample was 0.43. The genotypic frequencies of the different allele combinations according to race are demonstrated in Table 2 (chi-square, 2 df = 21.52, $p < 0.0001$).

Descriptive statistics for the body composition and exercise-related outcomes according to genotype are presented in Table 3. There were no significant differences in age or any of the absolute values for body composition and exercise variables when the subjects were compared according to genotype, except in ARMLM ($p = 0.0398$), LEGLM ($p = 0.0031$) and BIKEVO2-A ($p = 0.0333$) where, in all cases, homozygotes NC/NC had higher values.

Table 4 shows the results from the regression models where body composition parameters were the dependent variables. When evaluating the role of the presence/absence of the IGF-I₁₈₉ allele, neither FM, nor ARMFAT, LEGFAT or ARMLM were significantly associated with having the polymorphism after adjusting for lean body mass. In contrast, LBM and LEGLM were negatively associated with the presence of the allele, even after adjusting for AFADM. When the effects of specific genotypes were tested, significant results were observed for LBM and LEGLM with genotypic combination 189/NC and FM approached significance with genotypes 189/189. After adjusting for AFADM, only the associations between LBM and LEGLM with the heterozygous condition (189/NC) remained significant.

Results for strength and endurance performance are presented in Table 5. Leg strength was not associated with the presence/absence of IGF-I₁₈₉, or any genotype, with or without the inclusion of AFADM. However, carriers of the allele demonstrated a longer time on the treadmill, even after adjusting for AFADM. Likewise, heterozygotes (189/NC) had significantly longer TREADTIME, in models both with and without AFADM.

The IGF-I₁₈₉ polymorphism was negatively associated with oxygen uptake during cycling, indicating improved exercise economy (Table 6). The associations between oxygen uptake during cycling and IGF-I₁₈₉ remained after adjusting for admixture. Significant genotypic associations were also detected in the exercise economy measures.

Discussion

The results of this study suggest that the presence of IGF-I₁₈₉ contributes to reduced nonbone lean body mass in sedentary women, particularly in lower body limbs. Carriers of the IGF-I₁₈₉ allele showed more endurance as measured by time spent on the treadmill, independent of levels of African admixture. Consistent with the improved treadmill endurance and possibly contributing to this improved performance, individuals with IGF-I₁₈₉ consumed less oxygen even after adjusting for leg lean mass, suggesting a role of the polymorphism on exercise economy. This economy was independent of levels of African admixture. These findings suggest that carriers of IGF-I₁₈₉ would have a genetic predisposition to lower leg muscle mass, greater energy economy, and endurance performance.

Few other investigations have explored the relationship of IGF-I repeat polymorphism with body composition (24–26). Previous reports have shown that carriers of the IGF-I₁₈₉ alleles have lower fat mass. Contrary to the findings from Sun et al. (9), our study did not support associations with any fat mass measure independent of AFADM. The disparities in our results could have been a consequence of differences between the techniques used to assess body composition (underwater weighing vs DXA). On the other hand, our results suggested a role of IGF-I₁₈₉ on lean body mass, supporting the observations of lower FFM in carriers of this polymorphism (9). In addition, present results suggest that the lower LBM in carriers of the IGF-I₁₈₉ allele is manifested predominantly in the legs.

Previous investigations have shown that AA individuals have greater muscle mass and reduced VO_{2max} when compared to EA (27). The extent to which these racial differences are genetic has been an intriguing area of research among scientists and has just recently been explored (10,11). In the present study, there was a significant independent effect of AFADM on leg lean mass, supporting a genetic component to racial differences in this variable. Because differences

among the genotype frequencies were observed between AA and EA, we explored the interaction between AFADM and IGF-I₁₈₉ in the model where leg lean mass was the dependent variable. The result for the interaction was not significant ($P = 0.7438$), supporting a role of IGF-I₁₈₉ independent of AFADM. In the case of lean body mass and BIKEVO2-A, there were no significant effects of AFADM, but significant effects of IGF-I₁₈₉. This intriguing finding suggest that previously reported racial differences in various aspects of body composition, exercise economy and endurance performance may have been due to differences in the frequency of certain genetic polymorphisms or to the influence of non-genetic factors, such as social and cultural practices, but not to the effect of genetic ancestral background. Hence the most relevant finding of our study is that, independent of the degree of African admixture, individuals with IGF-I₁₈₉ are more likely to have low leg lean mass and to perform better in activities requiring exercise economy and endurance performance. Muscle strength and quality is also influenced by other factors non-tested in this study, e.g. muscle architecture, fiber type area, variation in encroachment of lipid into muscle and connective tissue, and availability of ATP in the vicinity of the myosin cross-bridge head. These factors may also contribute to observed differences in exercise economy and endurance phenotypes, and their contributions to these differences may be the bases for hypotheses for further exploration.

This study is strengthened by the inclusion of African admixture as a covariate. Racial and ethnic differences in measures of body composition and exercise performance have been described in the literature (28–30); the vast majority of them based on individual's self-classification. By using genetic admixture, we characterized the genetic factors underlying racial classification and their contribution, if any, to genotype-phenotype associations. Our results, however, are limited by a relatively small sample size that will only allowed testing for partial correlation greater than 0.20 at 70% power. This lack of power becomes limiting on hypothesis testing of certain models, particularly when testing putative relevant statistical interactions that may have provided insightful understandings the relationship between IGF-I₁₈₉ and measures of body composition, exercise performance and energy economy. For example, in various statistical models where the IGF-I₁₈₉ allelic association was significant, several genotypic associations were only significant in the heterozygous condition, but not in the homozygous 189/189, reflecting the lack of power in the latter group. In addition, our analyses included only two classifications: IGF-I₁₈₉ and noncarriers (NC). Possible relationships between IGF-I₁₈₉ and other alleles could not be analyzed because of power constraints. Future investigations with a larger sample size would be necessary to corroborate our findings and to further understand the contributions of other IGF-I polymorphisms.

In conclusion, the present study provides evidence toward IGF-I genetic polymorphisms influencing body composition and aspects of energy expenditure in humans. Although the mechanisms underlying the relationship between reduced leg lean mass and greater performance and economy are beyond the scope of this investigation, our findings provide the basis for innovative hypotheses and future experiments, including the consideration of the possible influence of IGF-I₁₈₉ on muscle fiber differentiation or the effect of the IGF-I₁₈₉ gene product in leg muscle mass.

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Table 1

Frequency distribution for the dinucleotide (CT)_n repeat polymorphism at the IGF-I gene in a sample of premenopausal women

Allele 2 (bp)											Total
Allele 1 (bp)	183	183	185	187	189	191	193	195	197	199	
	183	0	0	1	4	2	0	0	1	0	8
	185	0	1	1	3	4	0	1	0	0	10
	187	0	0	3	19	8	3	1	2	0	36
	189	0	0	0	19	20	12	1	0	0	52
	191	0	0	0	0	1	3	0	0	2	6
Total	193	0	0	0	0	1	1	0	1	0	2
		0	1	5	45	35	19	3	4	2	114

Table 2Number of individuals per genotype and genotypic frequencies (%) for IGF-1₁₈₉ according to race

Race	Genotypes			Total
AA	189/189 7 (10%)	189/NC 30 (42.9%)	NC/NC 33 (47.1%)	70 (100%)
EA	12 (27.3%)	29 (65.9%)	3 (6.8%)	44 (100%)

Table 3

General characteristics of the study sample stratified according to genotype classification with the presence of the IGF-I₁₈₉ polymorphism

Variable	189/189 (<i>n</i> = 19)		189/NC (<i>n</i> = 59)		NC/NC (<i>n</i> = 36)	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	35.4	4.7	33.5	5.7	35.0	5.9
Weight (kg)	74.6	11.7	71.3	10.1	74.1	10.4
BMI (kg/h ²)	27.1	2.9	26.7	2.7	26.6	2.9
AFADM	31.8	39.6	43.6	44.2	79.2	27.1
Body composition						
FM (kg)	42.0	5.3	38.9	6.0	38.3	7.6
LBM (kg)	38.4	5.5	37.7	3.8	39.8	4.4
ARMFAT (kg)	2.9	0.9	2.5	0.8	2.7	0.9
LEGFAT (kg)	13.45	3.6	11.6	2.9	12.2	3.7
ARMLM (kg) ^a	4.6	0.8	4.4	0.6	4.8	0.7
LEGLM (kg) ^a	13.7	2.1	13.5	1.6	14.8	1.6
Exercise variables						
LEGSTR (Newtons)	470.2	141.5	441.1	121.9	412.4	128.4
TREADTIME (min)	4.8	1.0	5.1	1.3	5.0	1.5
STAIRVO ₂ (ml/kg/min)	11.5	1.8	11.8	1.5	12.1	1.2
BIKEVO ₂ (ml/kg ⁻¹ min ⁻¹)	9.7	1.6	10.3	1.5	10.8	2.4
BIKEVO ₂ -A (ml/min) ^a	721.6	121.2	712.4	85.7	776.1	94.5

¹ NC, noncarriers,

² As determined by DXA.

Arm fat, [arm tissue (kg)*arm percent tissue fat]/100; leg fat, [leg tissue (kg)*leg percent tissue fat]/100; arm lean mass, [arm tissue (kg)*arm percent tissue lean mass]/100; leg lean mass, [leg tissue (kg)*leg percent tissue lean mass]/100; LEGSTR, isometric knee extension strength at 110 degrees; TREADTIME, time spent on treadmill during maximum VO₂ test; STAIRVO₂, the average steady-state VO₂ of the stair climbing VO₂; BIKEVO₂, the average steady-state VO₂ of the cycling adjusted by body mass; BIKEVO₂, the unadjusted average steady-state VO₂ of the cycling.

^a Represents significant differences among groups

Table 4

Estimates from the regression models for body composition parameters (kg) adjusted by lean body mass (LBM) and African genetic admixture (AFADM). The proportion of variance explained by the model is represented by the R-squared value (R^2)

Dependent Variable (R^2)	Parameter	Without admixture			With admixture		
		Estimate	SE	p value	Estimate	SE	p value
FM	LBM	-0.02	0.15	0.8991	-0.03	0.15	0.8302
	AFADM	-	-	-	-0.02	0.02	0.2630
	IGF-I ₁₈₉	1.45	1.44	0.3144	0.69	1.59	0.6664
				$R^2 = 0.12$			$R^2 = 0.02$
FM	LBM	0.01	0.15	0.9562	-0.05	0.15	0.7613
	AFADM	-	-	-	-0.02	0.02	0.3455
	189/NC	0.66	1.51	0.6626	0.06	1.64	0.9709
	189/189	3.71	1.93	0.0573	2.94	2.09	0.1622
				$R^2 = 0.04$			$R^2 = 0.05$
ARMFAT	LBM	0.09	0.02	<0.0001	0.09	0.02	<0.0001
	AFADM	-	-	-	-0.00	0.00	0.4630
	IGF-I ₁₈₉	0.12	0.17	0.5031	0.07	0.19	0.7202
				$R^2 = 0.21$			$R^2 = 0.21$
ARMFAT	LBM	0.09	0.02	<0.0001	0.09	0.02	<0.0001
	AFADM	-	-	-	-0.00	0.00	0.5787
	189/NC	0.01	0.18	0.9640	-0.02	0.20	0.9132
	189/189	0.39	0.23	0.0927	0.34	0.25	0.1779
				$R^2 = 0.23$			$R^2 = 0.24$
LEGFAT	LBM	0.21	0.07	0.0059	0.23	0.08	0.0079
	AFADM	-	-	-	0.00	0.01	0.7980
	IGF-I ₁₈₉	0.234	0.71	0.7412	0.28	0.78	0.7178
				$R^2 = 0.08$			$R^2 = 0.07$
LEGFAT	LBM	0.20	0.07	0.0069	0.20	0.07	0.0096
	AFADM	-	-	-	0.00	0.01	0.6352
	189/NC	0.24	0.74	0.7503	-0.16	0.81	0.8477
	189/189	1.44	0.94	0.1305	1.62	1.03	0.1195
				$R^2 = 0.11$			$R^2 = 0.11$
LBM	AFADM	-	-	-	-0.01	0.01	0.6634
	IGF-I ₁₈₉	-2.02	0.95	0.0361	-2.30	1.04	0.0299
				$R^2 = 0.04$			$R^2 = 0.05$
LBM	AFADM	-	-	-	-0.00	0.01	0.7096
	189/NC	-2.18	1.01	0.0342	-2.45	1.08	0.0265
	189/189	-1.60	1.31	0.2240	-1.80	1.41	0.2053
				$R^2 = 0.05$			$R^2 = 0.05$
ARMLM	LBM	0.11	0.01	<0.0001	0.11	0.01	<0.0001
	AFADM	-	-	-	0.00	0.00	<0.0001
	IGF-I ₁₈₉	-0.14	0.10	0.1748	0.04	0.10	0.6768
				$R^2 = 0.56$			$R^2 = 0.63$
ARMLM	LBM	0.11	0.01	<0.0001	0.11	0.01	<0.0001
	AFADM	-	-	-	0.00	0.00	<0.0001
	189/NC	-0.15	0.11	0.1576	0.01	0.11	0.8892
	189/189	-0.10	0.14	0.4737	0.13	0.14	0.3521
				$R^2 = 0.56$			$R^2 = 0.63$
LEGLM	LBM	0.35	0.02	<0.0001	0.35	0.02	<0.0001
	AFADM	-	-	-	0.01	0.00	<0.0001
	IGF-I ₁₈₉	-0.58	0.17	0.0006	-0.33	0.17	0.0469
				$R^2 = 0.83$			$R^2 = 0.86$
LEGLM	LBM	0.35	0.02	<0.0001	0.35	0.02	<0.0001
	AFADM	-	-	-	0.01	0.00	<0.0001
	189/NC	-0.59	0.18	0.0012	-0.37	0.17	0.0366
	189/189	-0.58	0.23	0.0121	-0.23	0.22	0.2935
				$R^2 = 0.83$			$R^2 = 0.86$

FM = fat mass, LBM = lean body mass, ARMFAT = (arm tissue (kg)*arm percent tissue fat)/100, LEGFAT = (leg tissue (kg)*leg percent tissue fat)/100, ARMLM = (arm tissue (kg)*arm percent tissue lean mass)/100, LEGLM = (leg tissue (kg)*leg percent tissue lean mass)/100

Table 5

Estimates from the regression models for muscle strength and exercise performance adjusted by African genetic admixture (AFADM), and body mass (WEIGHT) and leg lean mass (LEGLM) as appropriate. The proportion of variance explained by the model is represented by the R-squared value (R^2)

	Without admixture Parameter	Estimate	SE	<i>p</i> value	With admixture Estimate	SE	<i>p</i> value
LEGSTR	LEGLM	6.06	7.39	0.4142	9.32	7.58	0.2218
	AFADM	-	-	-	-0.49	0.34	0.1519
	IGF-I ₁₈₉	37.9	28.6	0.1874	26.9	30.57	0.3805
				$R^2 = 0.02$			$R^2 = 0.05$
LEGSTR	LEGLM	5.67	7.37	0.4441	8.75	7.61	0.2533
	AFADM	-	-	-	-0.45	0.34	0.1935
	189/NC	25.44	30.3	0.4037	18.1	32.0	0.5726
	189/189	67.40	37.6	0.0763	50.94	39.99	0.2061
				$R^2 = 0.04$			$R^2 = 0.06$
TREADTIME	WEIGHT	-0.09	0.01	<0.0001	-0.09	0.01	<0.0001
	LEGLM	0.46	0.08	<0.0001	0.48	0.09	<0.0001
	AFADM	-	-	-	-0.00	0.00	0.6666
	IGF-I ₁₈₉	0.67	0.25	0.0076	0.66	0.26	0.0149
				$R^2 = 0.35$			$R^2 = 0.35$
TREADTIME	WEIGHT	-0.09	0.01	<0.0001	-0.08	0.01	<0.0001
	LEGLM	0.45	0.08	<0.0001	0.47	0.09	<0.0001
	AFADM	-	-	-	-0.00	0.00	0.6132
	189/NC	0.76	0.26	0.0042	0.75	0.28	0.0078
	189/189	0.43	0.33	0.2043	0.39	0.35	0.2746
				$R^2 = 0.36$			$R^2 = 0.36$

LEGSTR, isometric knee extension strength at 110 degrees; TREADTIME, time spent on treadmill during maximum VO₂ test.

Table 6

Estimates from the regression models for exercise economy adjusted by African genetic admixture (AFADM), and leg lean mass (LEGLM). The proportion of variance explained by the model is represented by the *R*-squared value (R^2)

Variable	Parameter	Without admixture Estimate	SE	<i>p</i> value	With admixture Estimate	SE	<i>p</i> value
STAIRV O2	LEGLM	-0.1701	0.087	0.0529	-0.2196	0.087	0.0139
	AFADM	-	-	-	0.0015	0.003	0.7089
	IGF-I ₁₈₉	-0.5329	0.336	0.1163	-0.6043	0.353	0.0906
STAIRV O2				$R^2 = 0.05$			$R^2 = 0.08$
	LEGLM	-0.1669	0.087	0.0585	-0.2163	0.088	0.0162
	AFADM	-	-	-	0.001	0.004	0.7536
	189/NC	-0.4521	0.353	0.2098	-0.5593	0.371	0.1350
	189/189	-0.7291	0.446	0.1053	-0.7303	0.465	0.1200
BIKEVO2	LEGLM	-0.5215	0.108	$R^2 = 0.05$	-0.5735	0.110	$R^2 = 0.08$
	AFADM	-	-	<0.0001	0.0049	0.005	<0.0001
	IGF-I ₁₈₉	-1.4447	0.417	0.0008	-1.1541	0.443	0.0339
BIKEVO2				$R^2 = 0.22$			$R^2 = 0.26$
	LEGLM	-0.5151	0.107	<0.0001	-0.5647	0.1105	<0.0001
	AFADM	-	-	-	0.0099	0.005	0.0465
	189/NC	-1.2559	0.443	0.0056	-1.0236	0.463	0.0297
	189/189	-1.8978	0.550	0.0008	-1.6631	0.566	0.0105
BIKEVO2 -A	LEGLM	10.5894	6.08	$R^2 = 0.24$	9.007	6.329	$R^2 = 0.27$
	AFADM	-	-	0.0851	0.0671	0.2823	0.1581
	IGF-I ₁₈₉	-51.1138	23.646	0.0332	-52.4299	25.622	0.8127
BIKEVO2 -A				$R^2 = 0.11$			$R^2 = 0.11$
	LEGLM	10.5789	6.1224	0.0874	8.9265	6.3832	0.1655
	AFADM	-	-	-	0.0724	0.286	0.8005
	189/NC	-51.4650	25.278	0.0447	-53.7340	26.972	0.0494
	189/189	-50.2827	31.276	0.1114	-48.9436	33.465	0.1471
				$R^2 = 0.11$			

STAIRVO2, the average steady-state VO₂ of the stair climbing VO₂; BIKEVO2, the average steady-state VO₂ of the cycling VO₂ adjusted by body mass; BIKEVO2, the unadjusted average steady-state VO₂ of the cycling VO₂.